REMARKS

The title of the application is amended to be more descriptive of the invention.

Amendments to the claims

The claims 1-116 originally presented upon entry into the national stage are now all canceled. New claims 117-139 are presented for examination.

Support for claims 117 and 127 is provided by the specification at, e.g. page 21, line 3-12, in which inhibition of EOPA activity is shown to lead to inhibition of neurite sprouting and abnormal differentiation in neuronal precursor cells differentiated in culture. See also page 21, lines 24-33. At page 21, lines 16-33 complex formation between Lis1 or Disc1 and EOPA and its role in CNS development during embryogenesis and failure in developmental impairment are described.

The activity of EOPA in hydrolysis of bradykinin or neurotensin is described at page 12, lines 17-19.

Antibodies against EOPA are described in the original claim 45 and at pp. 10-11.

Peptide inhibitors of EOPA are described at page 13, lines 6 ff., and the requirement for thiol activation of EOPA is described at page 12, line 25. Mimetics of peptide substrates as inhibitors are described at page 13, lines 13-14 and enkephalin peptides as substrates are described at page 12, line 21. Bradykinin and neurotensin as substrates are described at page 12, lines 18-20. The particular amino acid sequences recited in the claims are those of the Leu^5 and Met^5 enkephalins (YGGFL and YGGFM, see Camargo et al. 1985, 1987 as cited in the specification) or of bradykinin (RPPGFSPFR) or neurotensin (ELYEBKPRRPYIL) (see, Juliano et al., *Biochem. Biophys. Res. Comm.* 173:647 (1990) at p. 650, copy provided with IDS of November 9, 2005).

Fluorogenic peptide substrates of EOPA are described at page 11, lines 8 ff. and the peptide Abz-GFAPFRQ-EDDnp is described at page 12, line 5.

Inhibition of EOPA by dynorphin derivatized by N-pys is described at, e.g. page 13, lines 5-20. Activity of bradykinin and neurotensin as inhibitors is described at page 12, lines 14-21.

Sequence Listing

A paper copy and CRF of a Sequence Listing are attached hereto and entry of the Sequence Listing into the application is requested. The Sequence Listing is provided for compliance with 37 CFR § 1.821-1.825 in view of newly presented claims.

No new matter is introduced by the Sequence Listing. As explained above, the short polypeptide sequences of enkephalins, bradykinin and neurotensin are the structures of the molecules so named. The cDNA and amino acid sequence of EOPA are provided; these sequences are referenced in the specification by their GenBank Accession numbers at page 4, lines 18-19.

The CRF of the Sequence Listing, filed herewith by EFS-web, is identical to the paper copy attached hereto, except that it lacks formatting information.

Response to restriction requirement

Claims 31, 62, 114-116 were pending after preliminary amendment and were considered for restriction.

The Examiner has required election in the present application among six groups of claims:

Group I, claims 31, 116, drawn to a human EOPA gene or cDNA. Classified in class 536, subclass 23.1;

Group II, claims 62, directed to a recombinant protein. Classified in class 530, subclass 350;

Group III, claims 114, drawn to a method of diagnosis by assessing level of EOPA mRNA expression. Classified in class 435, subclass 91.2;

Group IV, claims 114, drawn to a method of diagnosis by assessing level of EOPA protein expression. Classified in class 435, subclass 7.1;

Group V, claims 115, drawn to a method for compounding screening by assaying the compound for an activity as an inhibitor for neuropeptide inactivation by EOPA; and

Group VI, claims 115, drawn to a method for compounding screening by assaying the compound for an activity as an inhibitor for neuropeptide biotransformation by EOPA. Classification is to be determined depending on the nature of the assay.

For the purpose of examination of the present application, Applicants elect, with traverse, the subject matter of Group IV, directed to a method of diagnosis by assessing the level of EOPA protein expression.

Claims 118, 123-125 (to the extent the amount of Lis1 or Disc1 binding depends on the amount of EOPA present in a sample) and 126 read upon the elected invention. Claim 117 is generic.

Traverse is asserted as the present application is a national stage application of a PCT application. Accordingly, the Examiner should be applying Rule 13.1 of the PCT rules, not merely "restriction practice" according to U.S. practices. That is, the Examiner must identify a reference that destroys novelty of a "special technical feature" before a unity of invention requirement can be made.

The present claims are directed to methods of diagnosis of one of a number of disease conditions associated with changes in EOPA activity or level of expression, screening of a

compound for possible efficacy in treatment of such diseases, or improvements to (specific inhibition of EOPA vs. contributions to background activity by other, non-EOPA enzymes, thus improving sensitivity and strength of the diagnosis) or reagents (specific EOPA inhibitors and antibodies) for such assays. The Examiner has provided no reference that demonstrates that the connection of EOPA activity to the disease states mentioned in the claims was known in the art prior to filing of the present application. Thus, the instant restriction requirement is improper and must be withdrawn.

Furthermore, the present claim 117 serves as a linking claim that joins one or more of the restriction groups presented by the Examiner, in particular groups III and IV should be rejoined for consideration as within generic claim 117 should the subject matter of the claims of elected Group III be found allowable. Thus, at least all of claims 117 to 126 should be examined if the particular elected group of claims is found allowable.

Favorable action on the merits of the application is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Mark J. Nuell, Registration No. 36,623 at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

☒ Attached is a Petition for Extension of Time.

☒ Attached hereto is the fee transmittal listing the required fees.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____
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